REMARKS/ARGUMENTS

Claims 26-62 are pending in the application. In this Response, claims 26, 29, 40, 42-43, 45, 46, 48-49, 51-52, 54-55, 57 and 61 have been amended. The claim amendments are all entirely supported by the application as originally filed. Thus there is no issue of new matter. Furthermore, claims 27, 33-34, 44, 50, 53, 56, 58 and 60 have been cancelled from the application without prejudice or disclaimer to applicant's right to pursue patent protection for the subject matter of those claims in a subsequently-filed application.

Entry of the claim amendments is respectfully requested. Upon such entry, claims 26, 28-32, 35-43, 45-49, 51-52, 54-55, 57, 59 and 61-62 as amended, will be pending in this application.

Objection to the Specification

The Office Action states that the specification is objected to due to the lack of an Abstract of the disclosure.

In response to the objection applicant submits herewith an Abstract provided on a separate sheet as required under 37 C.F.R. 1.72(b). This submission is believed to overcome the objection to the specification, which should therefore be withdrawn.

Claim Rejections Under 35 U.S.C. 112

Claims 26-62 are rejected under 35 U.S.C. 112, first paragraph, due to an alleged failure to comply with the 'enablement' requirement of the statute.

In response to this ground of rejection, applicant has amended several of the claims contained in this application and submits that the claims are now all believed to comply with the 'enablement' requirements of 35 U.S.C. 112. In this context, moreover, the Examiner's attention is respectfully directed to the fact that amended claims 26-51 and 57-60 have been amended so as to be restricted to the particular subject matter elected (i.e., in the paper filed June 25, 2008) for further prosecution in this application. In particular, the term "alkaloid" has been amended to recite only a specific alkaloid, i.e., "chelidonine" and the expression "alkaloid derivative" has been restricted to "chelidonine derivative". These amendments are believed also to overcome the objection set forth in paragraph 9 on p. 5 of the Office Action of claims 26-51 and 57-60 for containing non-elected subject matter.

Further in response to the rejection based on an alleged lack of enablement and with regard to the Examiner's allegation that the written description of the invention does not contain an example of preparing chelidonine derivatives of Formula I, applicant respectfully disagrees and, in this regard, directs the Examiner's attention to the following.

To begin with, applicant wishes to clarify that the compound U-KRS described in the specification of the application is an example of a compound of Formula I. More specifically, U-KRS is a quaternary chelidonine derivative which is the reaction product of purified chelidonine with the alkylating agent tris(1-aziridinyl)phosphine sulphide (known as "thiotepa"). The process of preparing U-KRS, which thus provides an example of the preparation of a quaternary chelidonine derivative according to the presently pending amended claims is set forth in Example 3 provided in this application (see, e.g., p. 11, line 6 of the International Publication WO 2004/082698 A1 of the present application which clearly states that the precipitate obtained in Example 3 is thereafter referred to as U-KRS).

At p. 4, lines 25-30 the Publication WO 2004/082698 teaches that in the alkaloid derivatives, "the initially tertiary nitrogen atoms have been converted into quaternary nitrogens, wherein to the quaternary nitrogen a hydrogen residue or a residue originating from the alkylating agent [e.g., originating from thiotepa] is bound as a fourth ligand, the residue preferably being selected from the group consisting of methyl, ethyl and tris(1-aziridinyl)phosphine sulphide residue, or from a part of tris(1-aziridinyl)phosphine sulphide". Thus, since the origin of the fourth ligand (R1) of the presently claimed chelidonine derivatives is clearly stated in applicant's specification, no undue experimentation would thus be required to arrive at the presently claimed quaternary chelidonine derivatives of Formula I.

Additionally, the efficacy of a chelidonine derivative (i.e., U-KRS) in various medical applications is also disclosed in Examples 4 to 23 contained in the present specification. Applicant respectfully disagrees with the Examiner's view that Examples 4 to 23 do not present any results produced by the composition(s) recited in the present claims. For each biological test described in the subject Examples, the relevant material and method steps are disclosed. Applicant is convinced, based on this information, that one having an ordinary degree of skill in this field would be able to reproduce the subject Examples , which would result in such an individual obtaining the "relevant data" from these experiments as set forth in the portion headed "Results" for each of the Examples.

Still further, applicant notes that the Examiner objects to the recitation in the claims that the claimed composition(s) are useful in the prevention (prophylaxis) of certain disorders. In response, applicant has deleted the term "prophylaxis" from claims 57 and 61. It is believed that this amendment should overcome the Examiner's objection.

Based on the amendments to the claims and the remarks presented above, the Examiner is respectfully requested to reconsider and with draw the rejection of applicants' claims under 35 U.S.C. 112, first paragraph.

In addition to the §112, first paragraph, rejection discussed above, claims 56 and 60 have been rejected under 35 U.S.C. 112, second paragraph, for the reasons set forth in paragraph 7 on p. 5 of the Office Action. In response, applicant submits that both of the rejected claims have been canceled without prejudice or disclaimer in this Amendment and such cancellation is deemed to render moot the subject rejection. The Examiner is, thus, respectfully requested to reconsider and withdraw the rejection under 35 U.S.C. 112, second paragraph.

Claim Rejections Under 35 U.S.C. 102

Claims 52-62 are rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Zbierska, J. et al., *Herba Polonica*, Vol. 25, pp. 311-316 (1979). The cancellation of claims 53, 56, 58 and 6o without prejudice or disclaimer, renders moot the rejection of those claims. As to the remaining rejected claims, i.e., nos. 52, 54-55, 57, 59 and 61-62, the rejection is respectfully traversed.

In order to differentiate applicant's claimed chelidonine derivative as recited in independent claim 52, applicant has amended the subject claim to recite that the derivative is in water soluble form (as was originally recited in claim 53). The cited reference, however, in contrast discloses a compound, N-methylchelidonine methylsulfate, which is insoluble in water (see reference p. 311, third to last line). The reference does not disclose the subject compound, i.e., N-methylchelidonine methylsulfate in any water soluble form. Applicant, therefore respectfully submits that the claimed composition is thus novel over the disclosure contained in the cited reference as the reference does not disclose every feature recited in, e.g., independent claim 52.

The Examiner is, thus, respectfully requested to reconsider and withdraw the rejection under 35 U.S.C. 102(b) of applicant's claims 52-62.

Further to the above, notwithstanding that the Examiner has not raised a rejection of the subject claims under 35 U.S.C. 103, applicant respectfully submits that for the following reasons the claims are also believed not to be obvious over the Zbierska reference.

The present application teaches (see p. 2, lines 5-8 of WO 2004/082698) that the, "prior art methods for the manufacture of pharmacologically active chelidonine derivatives have in common that they require purification of the final product using inflammable or even explosive organic solvents". In contrast, it is the essence of the presently claimed compositions and methods that water or an aqueous solvent is used for washing the reaction product. This water washing step is not disclosed in the prior art.

More specifically, as taught for example at p. 3, lines 28-33 of the present application (WO 2004/082698) it was surprisingly found by the applicant that, "the washing step has a positive impact on the structure and composition of the reaction products in a way such that the efficiency such that the subsequent conversion step of the products into a water soluble form is augmented by up to 10 to 15 times compared to a process whereby the washing step is carried out using purely an organic solvent, thus remarkably improving the yield of the desired end product." (emphasis supplied). In sum, therefore, as the International Examiner noted in the International Preliminary Report on Patentability of the corresponding International Application WO 2004/082698 (in discussing the claims to the preparation of the alkaloid derivatives – see p. 9), "the applicant has discovered that by including this washing step with water after the alkylation step, the yield of the desired end product is unexpectedly increased compared to a washing step using organic solvents. Additionally, the water washing step removes any water-soluble components residing in the reaction mixture after the alkylating step. The increased yield obtained using this water-washing step gives rise to the acknowledgement of an inventive step of the presently claimed process."

Washing of the reaction product with water in the reaction process as recited, e.g., in claim 26 thus not only removes or reduces water soluble impurities, it additionally converts the reaction product into a state which, "facilitates the subsequent conversion step of the poorly water soluble or water-insoluble reaction products into water-soluble compounds" (see p. 3 of WO 2004/082698 lines 14-16), which effect was unexpected and not obvious from the prior art.

Applicant therefore submits that it would not be *prima facie* obvious to use water, instead of an organic solvent, in the washing step of the preparation process, since the prior art exhibited

no knowledge of the surprising catalytic effect of the water washing on the conversion of the reaction product into its water soluble form.

The presently claimed alkaloid reaction product (which has been washed with water) is also not obvious over the prior art due to the fact that it exhibits improved properties relative to the state of the art alkaloid reaction product, which has been washed with an organic solvent. The present application teaches (see, e.g., WO 2004/082698, p. 6 at lines 11-14) that, "some water-soluble toxic alkaloids which contribute to adverse reactions in medical applications and might even cause cirrhosis of the liver are removed with the aqueous phase from the synthesis mixture or their concentrations are reduced." In addition, on the same page, lines 3-5 recite that, "thiotepa decomposes in water [but not in an organic solvent] [and therefore] the unconverted residue of thiotepa present in excess after the reaction can be removed from the organic phase by this measure."

The alkaloid reaction product thus claimed in the present application is, therefore, an improved composition as compared to the known state of the art reaction products which are not as free from undesired toxic side products.

Further to the above, the reaction products that remain after the water washing step have reduced negative side effects when used the material is used in medical applications due to a reduction in the amount of toxic components. At p. 2., lines 18-21 the published application (WO 2004/082698) teaches that be converting the alkaloid derivatives into water-soluble salts, "injectable pharmaceutical preparations of low toxicity and having a broad spectrum of therapeutic activity" are obtained.

In addition, applicant submits that it seems clear that one having an ordinary level of skill in the relevant art, e.g., a medical doctor or a physician, would choose the presently claimed composition(s) over those known in the prior art due to the reduced content of undesirable by-products as contained in the claimed material(s) and the fact that the presently claimed composition(s) thus may applied and administered even to sensitive individuals which otherwise might have developed allergic reactions to the by-products still contained in the material according to the prior art.

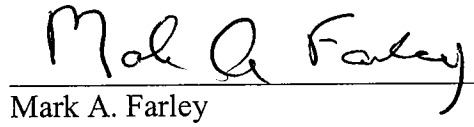
Summary

Based on the claim amendments and arguments presented above, the Examiner is respectfully requested to withdraw all of the objections and rejections set forth in the present Office Action concerning this application and to issue a Notice of Allowance for the remaining claims of the application.

THIS CORRESPONDENCE IS BEING SUBMITTED ELECTRONICALLY THROUGH THE PATENT AND TRADEMARK OFFICE EFS FILING SYSTEM ON March 3, 2009.

MAF:stb

Respectfully submitted,



Mark A. Farley
Registration No.: 33,170
OSTROLENK, FABER, GERB & SOFFEN, LLP
1180 Avenue of the Americas
New York, New York 10036-8403
Telephone: (212) 382-0700